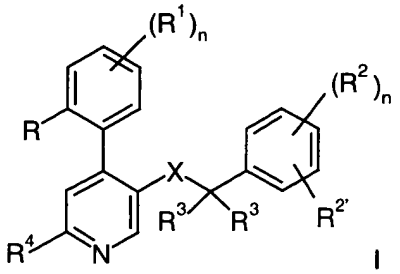
Claims

1. A method of treating benign prostatic hyperplasia in a mammal by administering to the mammal an effective amount of an NK-1 receptor antagonist.

2. The method according to claim 1, wherein the NK-1 receptor antagonist is a compound of the general formula (I)



I

wherein

R is hydrogen, lower alkyl, lower alkoxy, halogen or trifluoromethyl;

R^1 is hydrogen or halogen; or

R and R^1 may be together –CH=CH-CH=CH-;

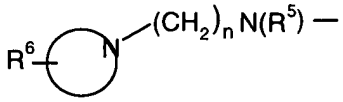
R^2 and $R^{2'}$ are independently from each other hydrogen, halogen, trifluoromethyl, lower alkyl, lower alkoxy or cyano; or

R^2 and $R^{2'}$ may be together –CH=CH-CH=CH-, optionally substituted by one or two substituents selected from lower alkyl, halogen or lower alkoxy;

R^3 is, independently from each other if occurring twice, hydrogen, lower alkyl or may, if occurring twice, form together with the carbon atom to which they are attached a cycloalkyl group;

R^4 is hydrogen, $-N(R^5)_2$, $-N(R^5)(CH_2)_nOH$, $-N(R^5)S(O)_2$-lower alkyl, $-N(R^5)S(O)_2$-phenyl, $-N=CH-N(R^5)_2$, $-N(R^5)C(O)R^5$, a cyclic tertiary amine of the group

or the group



;

or R^4 is $-(C\equiv C)_nR^7$ or $=(CR'=CR'')_nR^7$

wherein R^7 is

a) halogen,

b) cyano, or the following groups:

c) $-(CR'R'')_n-R^8$,

d) $-C(O)NR'R''$,

e) $-C(O)O(CH_2)_nR^8$,

f) $-C(O)R^8$,

g) $-N(OH)-(CH_2)_nR^8$,

h) $-NR'C(O)-(CH_2)_nR^8$,

i) $-N[C(O)-R']_2$,

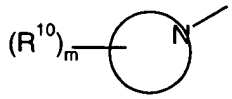
j) $-OR^9$,

k) $-(CH_2)_n-SR^9$, $-(CH_2)_n-S(O)R^9$, or $-(CH_2)_n-S(O)_2R^9$,

l) aryl, optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R'', nitro, $-(CH_2)_mOR'$, -C(O)NR'R'', -C(O)OR' or -C(O)R',

m) is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and may be optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R'', nitro, $-(CH_2)_mOR'$, -C(O)OR', -C(O)NR'R'' or -C(O)R',

n) is a five or six membered saturated cyclic tertiary amine of the group



which may contain one additional heteroatom, selected from N, O or S,

R'/R'' are independently from each other hydrogen, hydroxy, lower alkyl, cycloalkyl or aryl, wherein the lower alkyl, cycloalkyl or aryl group may be optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'''R'''', nitro, $-(CH_2)_mOR'''$, -C(O)NR'''R'''', -C(O)OR''' or -C(O)R''',

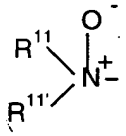
R'''/R'''' are independently from each other hydrogen, lower alkyl, cycloalkyl or aryl,

R^8 is hydrogen, cyano, hydroxy, halogen, trifluoromethyl, -C(O)OR', -OC(O)R' or aryl, optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R", nitro, $-(CH_2)_mOR'$, -C(O)NR'R", -C(O)OR' or -C(O)R', or is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and may be optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R", nitro, $-(CH_2)_mOR'$, -C(O)NR'R", -C(O)OR' or –C(O)R',

R^9 is hydrogen, lower alkyl, trifluoromethyl, or aryl, wherein the lower alkyl or aryl group may be optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R", nitro, -C(O)NR'R", $-(CH_2)_mOR'$, -C(O)OR' or –C(O)R', or is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and may be optionally substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, -NR'R", nitro, $-(CH_2)_mOR'$, -C(O)NR'R", -C(O)OR' or –C(O)R',

R^{10} is $-C(O)-(CH_2)_nOH$ or an oxo group;

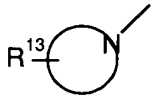
or R^4 is an N-oxide of the general formula



wherein R^{11} and $R^{11'}$ are independently from each other $-(CH_2)_pOR^{12}$ or lower alkyl, wherein R^{12} is hydrogen, lower alkyl or phenyl;

or

R^{11} and $R^{11'}$ form together with the N-atom to which they are attached a cyclic tertiary amine of the group



wherein R^{13} is hydrogen, hydroxy, lower alkyl, lower alkoxy, $-(CH_2)_pOH$, $-COOR^3$, $-CON(R^3)_2$, $-N(R^3)CO$-lower alkyl or $-C(O)R^3$;

R^5 is, independently from each other, hydrogen, C_{3-6}-cycloalkyl, benzyl, phenyl or lower alkyl;

R^6 is hydrogen, hydroxy, lower alkyl, $-(CH_2)_nCOO$-lower alkyl, $-N(R^5)CO$-lower alkyl, hydroxy-lower alkyl, cyano, $-(CH_2)_nO(CH_2)_nOH$, -CHO or a 5-or 6 membered heterocyclic group, optionally bonded via an alkylene group;

X is $-C(O)N(R^5)-$, $-(CH_2)_pO-$, $-O(CH_2)_p-$, $-(CH_2)_pN(R^5)-$, $-N(R^5)C(O)-$, or $-N(R^5)(CH_2)_p-$;

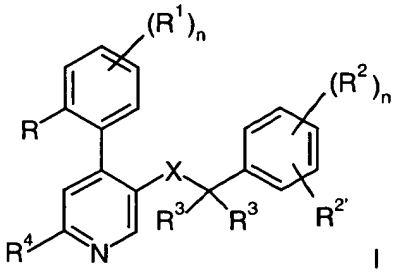
n is 0, 1, 2, 3 or 4;

m is 1 or 2; and

p is 1, 2 or 3;

and the pharmaceutically acceptable acid addition salts and the prodrugs thereof.

3. The method according to claim 1, wherein the NK-1 receptor antagonist is a compound of general formula (I)



I

wherein

R is hydrogen, lower alkyl, lower alkoxy, halogen or trifluoromethyl;

R^1 is hydrogen or halogen; or

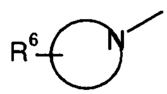
R and R^1 may be together –CH=CH-CH=CH-;

R^2 and $R^{2'}$ are independently from each other hydrogen, halogen, trifluoromethyl, lower alkoxy or cyano; or

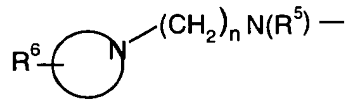
R^2 and $R^{2'}$ may be together –CH=CH-CH=CH-, optionally substituted by one or two substituents selected from lower alkyl or lower alkoxy;

R^3 is hydrogen, lower alkyl or form a cycloalkyl group;

R^4 is hydrogen, $-N(R^5)_2$, $-N(R^5)(CH_2)_nOH$, $-N(R^5)S(O)_2$-lower alkyl, $-N(R^5)S(O)_2$-phenyl, $-N=CH-N(R^5)_2$, $-N(R^5)C(O)R^5$ or a cyclic tertiary amine of the group



or the group



;

R^5 is, independently from each other, hydrogen, C_{3-6}-cycloalkyl, benzyl or lower alkyl;

R^6 is hydrogen, hydroxy, lower alkyl, $-(CH_2)_nCOO$-lower alkyl, $-N(R^5)CO$-lower alkyl, hydroxy-lower alkyl, cyano, $-(CH_2)_nO(CH_2)_nOH$, -CHO or a 5-or 6 membered heterocyclic group, optionally bonded via an alkylene group;

X is $-C(O)N(R^5)-$, $-(CH_2)_mO-$, $-(CH_2)_mN(R^5)-$, $-N(R^5)C(O)-$, or $-N(R^5)(CH_2)_m-$;

n is 0, 1, 2, 3 or 4; and

m is 1 or 2;

and the pharmaceutically acceptable acid addition salts and the prodrugs thereof.

4. The method according to claim 2 or claim 3, wherein the NK-1 receptor antagonist is a compound of general formula (I), wherein X is $-C(O)N(R^5)-$ and R^5 is methyl, ethyl or cyclopropyl.

5. The method according to claim 4, wherein the compound is selected from the group consisting of

N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-(2-chloro-phenyl)-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-(2-trifluoromethyl-phenyl)-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-(2-fluoro-phenyl)-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-(2-methoxy-phenyl)-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-phenyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-ethyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-cyclopropyl-4-o-tolyl-nicotinamide,
N-[1-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-di-fluorobenzyl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-di-chlorobenzyl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(4-methyl-piperazin-1-yl)-4-o-tolyl-nicotinamide,
2'-methyl-5-(4-methyl-piperazin-1-yl)-biphenyl-2-carboxylic acid-(3,5-bis-trifluoromethyl-benzyl)-methyl-amide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(4-methyl-piperazin-1-yl)-4-naphthalen-1-yl-nicotinamide,
(4-{5-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4-o-tolyl-pyridin-2-yl}-piperazin-1-yl)-acetic acid ethyl ester,
5'-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4'-o-tolyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(4-propyl-piperazin-1-yl)-4-o-tolyl-nicotinamide,
(RS)-6-[3-(acetyl-methyl-amino)-pyrrolidin-1-yl]-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-[methyl-(2-morpholin-4-yl-ethyl)-amino]-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-morpholin-4-yl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-thiomorpholin-4-yl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(1-oxo-1λ^4-thiomorpholin-4-yl)-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-piperazin-1-yl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-N-methyl-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-cyanomethyl-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-{4-[2-(2-hydroxy-ethoxy)-ethyl]-piperazin-1-yl}-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(4-[1,2,4]oxadiazol-3- yl-methyl-piperazin-1-yl)-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-[4-(5-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-yl-methyl)-piperazin-1-yl]-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-formyl-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide, and
N-methyl-N-(2-methyl-naphthalen-1-yl-methyl)-6-morpholin-4-yl-4-o-tolyl-nicotinamide;

or a pharmaceutically acceptable acid addition salt thereof.

6. The method according to claim 2 or claim 3, wherein the NK-1 receptor antagonist is a compound of general formula (I), wherein X is $-N(R^5)-C(O)-$ and R^5 is hydrogen or methyl.

7. The method according to claim 6, wherein the compound is selected from the group consisting of
2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-N-methyl-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(4-fluoro-2-methyl-phenyl)-6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-N-methyl-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl-N-methyl-N-(4-o-tolyl-pyridin-3-yl)-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-(4-o-tolyl-pyridin-3-yl)-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(4-o-tolyl-pyridin-3-yl)-acetamide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(4-o-tolyl-pyridin-3-yl)-propionamide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)-isobutyramide,
2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-morpholin-4-yl-

pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-{6-[methyl-(2-morpholin-4-yl-ethyl)-amino]-4-o-tolyl-pyridin-3-yl}-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-pyrimidin-2-yl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-dimethylamino-pyridin-3-yl]-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-piperazin-1-yl-4-o-tolyl-pyridin-3-yl)-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(4-hydroxy-4'-o-tolyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl)-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-{6-[(2-hydroxy-ethyl)-methyl-amino]-4-o-tolyl-pyridin-3-yl}-N-methyl-isobutyramide,

(R)-2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxy-pyrrolidin-1-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)-acetamide, and

[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-[4-(4-fluoro-2-methyl-phenyl)-6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-methylamine;

or a pharmaceutically acceptable acid addition salt thereof.

8. The method according to claim 4, wherein the compound is selected from the group consisting of

N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-6-[1,2,4]triazol-1-yl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-(2-hydroxy-ethylamino)-N-methyl-4-o-tolyl-nicotinamide,

4-hydroxy-4'-o-tolyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide,

4-(2-hydroxy-ethoxy)-4'-o-tolyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide,

(R)-N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-hydroxy-pyrrolidin-1-yl)-N-methyl-4-o-tolyl-nicotinamide, and

4'-(2-chloro-phenyl)-4-hydroxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

or a pharmaceutically acceptable acid addition salt thereof

9. The method according to claim 6, wherein the compound is selected from the group consisting of

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2-hydroxy-ethylamino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2,3-dihydro-[1,4]oxazin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

N-(6-acetylamino-4-o-tolyl-pyridin-3-yl)-2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-isobutyramide,

N-[6-(acetyl-methyl-amino)-4-o-tolyl-pyridin-3-yl]-2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-isobutyramide,

cyclopropanecarboxylic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-yl)-amide,

cyclopropanecarboxylic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-yl)-methyl-amide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-imidazol-1-yl-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide, and

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(2-hydroxy-ethylamino)-pyridin-3-yl]-N-methyl-isobutyramide;

or a pharmaceutically acceptable acid addition salt thereof

10. The method according to claim 2 or 3, wherein the NK-1 receptor antagonist is a compound of general formula (I), wherein R^4 is $-(C\equiv C)_nR^7$ or $-(CR'=CR'')_nR^7$.

11. The method according to claim 10, wherein the NK-1 receptor antagonist is a compound according to formula (I), wherein in R^4 is $-(C\equiv C)_nR^7$ or $-(CR'=CR'')_nR^7$ and X is $-C(O)N(CH_3)-$ and $(R^2)_n$ is 3,5-di-CF_3.

12. The method according to claim 11, wherein the compound is selected from the group consisting of

N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxyacetyl-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-chloro-N-methyl-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-cyanomethyl-N-methyl-4-o-tolyl- nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-iodo-N-methyl-4-o-tolyl-nicotinamide,
4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide,
5-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4-o-tolyl-pyridine-2-carboxylic acid methyl ester,
N-(3,5-bis-trifluoromethyl-benzyl)-6-hydroxymethyl-N-methyl-4-o-tolyl-nicotinamide,
6-(5-acetyl-thiophen-2-yl)-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-nicotinamide,
4-o-tolyl-1',2',3',6'-tetrahydro-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide,
N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxymethyl-phenyl)-N-methyl-4-o-tolyl-nicotinamide,
2'-methyl-4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(3-methyl-[1,2,4]oxadiazol-5-yl)-4-o-tolyl-nicotinamide,
6-(3-amino-prop-1-ynyl)-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-nicotinamide,
(RS)-N-(3,5-bis-trifluoromethyl-benzyl)-6-(2-hydroxy-ethanesulfinylmethyl)-N-methyl-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(1-methyl-1H-imidazol-2-yl-sulfanylmethyl)-4-o-tolyl-nicotinamide,
(RS)-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfinyl)-4-o-tolyl-nicotinamide,
N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfonyl)-4-o-tolyl-nicotinamide, and
N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-hydroxy-propoxy)-N-methyl-4-o-tolyl-nicotinamide;

or a pharmaceutically acceptable acid addition salt thereof.

13. The method according to claim 10, wherein the NK-1 receptor antagonist is a compound of general formula (I), wherein R^4 is $-(C\equiv C)_nR^7$ or $-(CR'=CR'')_nR^7$ and X is $-N(CH_3)C(O)-$ and $(R^2)_n$ is 3,5-di-CF_3.

14. The method according to claim 13, wherein the compound is selected from the group consisting of

2-(3,5-bis-trifluoromethyl-phenyl)-N-{6-[hydroxy-(2-hydroxy-ethyl)-amino]-4-o-tolyl-pyridin-3-yl}-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(3-oxo-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide,

acetic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-ylcarbamoyl)-methyl ester,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2-hydroxy-acetylamino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(hydroxyacetyl-methyl-amino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2,5-dioxo-pyrrolidin-1-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

cyclopropanecarboxylic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-yl)-cyclopropanecarbonyl-amide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-chloro-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-2'-methyl-[2,4']bipyridinyl-5-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-ethynyl-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxymethyl-isoxazol-5-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxy-prop-1-ynyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide, and

(RS)-2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-methoxy-benzenesulfinyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide;

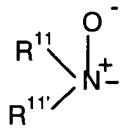
or a pharmaceutically acceptable acid addition salt thereof.

15. The method according to claim 10, wherein the NK-1 receptor antagonist a compound of general formula (I), wherein R^4 is $-(C\equiv C)_nR^{11'}$ or $-(CR'=CR'')_nR^{11'}$ and R^3 and $R^{3'}$ are both methyl and R is chloro.

16. The method according to claim 15, wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-{4-(2-chloro-phenyl)-6-[hydroxy-(2-hydroxy-ethyl)-amino]-pyridin-3-yl}-N-methyl-

isobutyramide or is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(3-oxo-morpholin-4-yl)-pyridin-3-yl]-N-methyl-isobutyramide or is a pharmaceutically acceptable acid addition salt thereof.

17. The method according to claim 2 or 3, wherein the NK-1 receptor antagonist is a compound of general formula (I), wherein R^4 is an N-oxide of the general formula



and X is $-C(O)N(R^5)-$ and R^5 is methyl or X is $-N(R^5)-C(O)-$ and R^5 is hydrogen or methyl.

18. The method according to claim 17, wherein the compound is selected from the group consisting of

4-{5-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4-o-tolyl-pyridin-2-yl}-4-oxy-piperazine-1-carboxylic acid tert-butyl ester,

5'-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4'-o-tolyl-1-oxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid ethyl ester,

(RS)-6-[3-(acetyl-methyl-amino)-1-oxo-pyrrolidin-1-yl]-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-(1,1-dioxo-1λ^6-4-oxy-thiomorpholin-4-yl)-N-methyl-4-o-tolyl-nicotinamide,

N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-formyl-1-oxy-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide,

N-methyl-N-(2-methyl-naphthalen-1-yl-methyl)-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

N-methyl-6-(4-oxy-morpholin-4-yl)-N-naphthalen-1-yl-methyl-4-o-tolyl-nicotinamide,

N-(2-methoxy-naphthalen-1-yl-methyl)-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

N-(2-methoxy-benzyl)-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

N-(5-chloro-2-methoxy-benzyl)-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-

nicotinamide,

N-(2-chloro-5-methoxy-benzyl)-N-methyl-6-morpholin-4-yl-4-o-tolyl-nicotinamide,

N-methyl-6-(4-oxy-morpholin-4-yl)-N-pentafluorophenylmethyl-4-o-tolyl-nicotinamide,

N-methyl-6-(4-oxy-morpholin-4-yl)-N-naphthalen-2-yl-methyl-4-o-tolyl-nicotinamide,

N-[2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

N-(1,4-dimethoxy-naphthalen-2-yl-methyl)-N-methyl-6-(4-oxy-morpholin-4-yl)-4-o-tolyl-nicotinamide,

5'-[(3,5-bis-trifluoromethyl-benzyl)-methyl-carbamoyl]-4'-o-tolyl-1-oxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carboxylic acid,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(4-oxy-morpholin-4-yl)-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4'-(2-chloro-phenyl)-1-oxy-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-oxy-dimethylamino-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-oxy-dimethylamino-pyridin-3-yl]-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-1-(4-hydroxy-1-oxy-4'-o-tolyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl)-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-{6-[(2-hydroxy-ethyl)-1-oxy-methyl-amino]-4-o-tolyl-pyridin-3-yl}-N-methyl-isobutyramide,

(R)-2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxy-1-oxy-pyrrolidin-1-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide,

2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-acetamide,

2-(3,5-dimethoxy-phenyl)-N-methyl-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-acetamide, and

2-(3-fluoro-5-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-acetamide;

or a pharmaceutically acceptable acid addition salt thereof.

19. The method according to claim 2 or 3, wherein the NK-1 receptor antagonist is 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)-isobutyramide or is 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-oxy-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide or is a pharmaceutically acceptable acid addition salt thereof.

20. The method according to claim 2 or 3, wherein the NK-1 receptor antagonist is 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide, or 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide or pharmaceutically acceptable acid addition salts thereof.

21. The method according to claim 1, wherein the NK-1 receptor antagonist is a compound selected from the group of NK-1 receptor antagonists under drug development designated GR205171, HSP-117, L 703,606, L 668,169, LY 303241, LY 306740, MK-869, R-544, Spantide III, WIN-62,577, GR 103,537, L 758,298, NKP608, CGP49823, CP-96,345, CP-99,994, CP-122,721, FK 888, GR203040, GR 82334, GR 94800, L 732,138, L 733,060, L 742,694, L 754,030, LY 303870, MEN 11149, PD 154075, RP-67580, RPR 100893, Spendide, Spantide II, SR140333, WIN-41,708, WIN-62,577, SR-48,968, L-659,877, MEN 10627, SR 144190, GR 94800, SR-142,801, R820, R486, SB 222200, L 758,298, NK-608, CGP 47899 and MEN 11467; or is a pharmaceutically acceptable acid addition salt thereof.

22. The method of Claim 1, wherein the NK-1 receptor antagonist has a pKi of greater than 7.

23. The method of Claim 22, wherein the NK-1 receptor antagonist has a pKi of between 8 and 10.

24. The method of Claims 1-3 and 22-23, wherein the mammal is a human.

25. A pharmaceutical composition comprising one or more NK-1 receptor antagonists as defined in Claim 21 and a pharmaceutically acceptable excipient for the treatment of benign prostatic hyperplasia.

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